compound. On the contrary, Table 2 (as relied upon by the Examiner) does not show this type of variation. In fact, while the ratio of the inhibitory efficacy of Applicants' compound to the reference compound is nearly 3 to 1, the ratio of compound 2 to compound 3 (in Table 2) is 1.1 to 1. Thus, the ratio of these values is nearly 1:1. Accordingly, it is untenable to assert that this Table teaches that the variation is considerable, and thus that Applicants' results are not unexpected.

Additionally, the Examiner refers to EP 1 236 725 (EP '725), and asserts that this reference teaches that inhibition of PDE activity varies and that the range of variation is not considered to be unexpected. Specifically, the Examiner refers to Table 1 of EP '725, and states that some of the compounds differ only in the alkyl chain and the activity changes.

Initially, Applicants note that the teachings in EP '725 upon which the Examiner relies relate to compounds which differ by the length of an alkyl chain (but which all do contain an alkyl chain). On the contrary, the distinction between the compound of the cited references and Applicants' claimed compound is the actual presence of a methylene chain. Thus, Applicants assert that this comparison is untenable.

However, for the sake of completeness, Applicants provide the following additional comments.

Upon careful review of the Table referred to by the Examiner, Applicants note the following: when the alkyl group increases (from methyl to ethyl, to propyl, etc.) the value of IC_{50} (μm) increases. For example, it appears that the compounds of Example 4, 6, 8, 15 and 17 differ only in the alkyl chain, methyl, ethyl, propyl, butyl and pentyl, respectively. Although the value for Example 4 is not provided, the values for the other Examples are as follows: 0.16 (Example 6), 0.44 (Example 8), 1.4 (Example 15) and 2.2 (Example 17).

Similarly, please note the values for Examples 2, 5, 7, 14 and 16, which also appear to differ only in increasing alkyl chain length: 0.11 (Example 2), 0.06 (Example 5), 1.3 (Example 7), 1.5 (Example 14) and 1.9 (Example 16). Applicants acknowledge that Example 5 (ethyl) has a lower value than Example 2 (methyl). However, given the consistency of the other results, it is appears that the IC_{50} value increases with an increased alkyl chain length. Thus, the PDE IV inhibitory efficacy appears to decrease as the length of the alkyl chain increases.

As discussed in detail before, the difference between Applicants' claimed compound(s) and the compound of the cited references is the presence of a methylene linker in Applicants' claimed compound. As also previously discussed, the PDE IV inhibitory efficacy of Applicants' compound

(IC_{50} = 0.084 μM) is about three times higher than the efficacy of the compound of the cited reference (IC_{50} = 0.25 μM). Thus, contrary to the results discussed above (in EP '725), the increase in alkyl length, from zero in the cited reference, to one (methylene) in Applicants' claimed compound, actually improves the PDE IV efficacy.

Thus, even if one skilled in the art were to look to the teachings of EP '725 to determine whether Applicants' results were unexpected, the definitive answer would be yes, since the presence of methylene improves efficacy, rather than decreases efficacy, as suggested by the reference.

For the above reasons, Applicants assert that the results of the present invention are unexpected. Accordingly, the rejection of record is untenable and should be withdrawn.

Conclusion

Therefore, in view of the remarks, it is submitted that the ground of rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

If, after reviewing this Amendment, the Examiner feels there are any issues remaining which must be resolved before the application can be passed to issue, the Examiner is respectfully requested to contact the undersigned by telephone in order to resolve such issues.

Respectfully submitted,

Hashime KANAZAWA et al.

By: _____

Amy E. Schmid
Registration No. 55,965
Attorney for Applicants

AES/emj
Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
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